



NASA STTR 2004 Phase I Solicitation

T5 Johnson Space Center

The Johnson Space Center's chief mission is the expansion of a human presence in space through exploration and the utilization of space for the benefit of mankind. The Center is also the lead center for curation and research of astromaterials (including Lunar rocks and other specimens), the International Space Station, the Space Shuttle, home to the Mission Control Center and to the NASA astronaut corps, and leads the development, testing, production and delivery of U.S. human spacecraft.

Subtopics

T5.01 Understanding and Utilizing Gravitational Effects on Molecular Biology and for Medical Applications

Lead Center: JSC

The microgravity environment enables scientists to perform unique studies on metabolic and functional changes *in* cells, and modified growth of multiple cells for artificial tissue development and behavior. NASA has developed novel rotating bioreactor technologies to model microgravity effects on cultures of suspended and anchorage-dependent cells and tissues. The spin-off from the NASA research has been the use of these novel culture methods for Earth-based research into mechanisms of enhancing cytokine and hormone secretions, production of 3-D tissue spheroids, interactions of cancer cells and normal cells *in* co-culture, and molecular mechanisms of altered immune cell functions, bone formation, and special uses of stem cells. The current focus is on development of new methods for enhancing production of commercial products from cultured cells for medicine and biotechnology applications. NASA cell science research includes development of space bioreactors for culture of fragile human cells; mechanisms for enhancing production of IFNs and cytokines from human white blood cells, near-infrared light mechanisms that stimulate wound healing and bone formation, and also for photodynamic therapy for local treatment of solid tumors; and tissue engineering systems which grow 3-D tissue constructs. New systems have been developed for microencapsulation of drugs and cells for transplantation *in* concert with the new culture systems for *in vitro* testing of the effectiveness of new drug combinations and biomodulators, and methods for measuring metastatic potential of tumor biopsies, and new tests for changes *in* specific cellular immune functions of persons under physiological stress. New fluorescent and bioluminescence imaging technologies are being developed to aid *in* the real-time assessment of these various effects on cultured cells *in* bioreactors and then applied to clinical tests especially for monitoring treatments for cancer.

Specific areas of interest are:

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- New methods for culturing mammalian cells in bioreactors, including advanced bioreactor design and support systems; miniature sensors for measurement of pH, oxygen, carbon dioxide, glucose, glutamine, and metabolites; and microprocessor controllers. Neural fuzzy logic network systems for the control of mammalian cell culture systems. Methods to minimize biofilm formation on fluid-handling components, sensors, and bioreactors. Spectroscopic and biochemical analysis of biofilm formed in bioreactors. Micro-scale bioreactors for biomonitoring of radiation and other external stressors.
 - Technologies that allow automated biosampling and biospecimen collection, handling, preservation and fixation, and processing in cellular systems. Methods for separation and purification of living cells, proteins, and biomaterials, especially those using electrokinetic or magnetic fields that obviate thermal convection and sedimentation, enhance phase partitioning, or use laser light and other force fields to manipulate target cells or biomaterials.
 - Techniques or apparatus for macro-molecular assembly of biological membranes, biopolymers, and molecular bioprocessing systems; biocompatible materials, devices, and sensors for implantable medical applications including molecular diagnostics, *in vivo* physiological monitoring and microprocessor control of prosthetic devices.
 - Methods and apparatus that allow microscopic imaging including hyperspectral fluorescent, scattering and absorption imaging and biophysical measurements of cell functions, effects of electric or magnetic fields, photoactivation, and testing of drugs or biocompatible polymers on live tissues. Integrated instrumentation for separation and purification of RNA, DNA, and proteins from cells and tissues.
 - Quantitative applications of molecular biology, fluorescence imaging and flow cytometry, and new methods for measurement of cell metabolism, cytogenetics, immune cell functions, DNA, RNA, oligonucleotides, intracellular proteins, secretory products, and cytokine or other cell surface receptors. Means to enhance and augment genomics and proteomics techniques, including molecular and nanoscale tools. Small-scale mass spectrometers. Development of novel fluorophores that tag proteins mediating cellular function, particularly those that can be excited using solid-state lasers.
 - Micro-encapsulation of drugs, radiocontrast agents, crystals, and the development of novel drug delivery systems wherein immiscible liquid interactions, electrostatic coating methods, and drug release kinetics from microcapsules or liposomes can be altered under microgravity to better understand and improve manufacturing processes on Earth.
 - Miniature bioprocessing systems, which allow for precise control of multiple environmental parameters such as low-level fluid shear, thermal, pH, conductivity, external electromagnetic fields, and narrow-band light for fluorescence or photoactivation of biological systems.
 - Novel low temperature sample storage methods (-80°C and -180°C) and biological sample preservation methods. Methods to reduce launch/return mass of biological samples and support reagents.
 - DNA template for molecular wiring that permits macro- to nanoscale connectivity. Nanoscale electronics based on self-assembling protein-based molecular structures.
 - Computer models and software that better handle large numbers of coupled reactions in cell science systems.
 - Tools and techniques to study mechanical properties of the cell: subcellular rheology, cell adhesion, affect of shear flow, affects of direct mechanical perturbation. Tools and techniques to facilitate multiple simultaneous probing and analyzing of a cell or subcellular region (examples include atomic force microscope coupled with microelectrode or micro-Raman, Optical trap).
 - Nanosensors for subcellular measurements: ultra-microelectrodes with less than 1micron diameter including cladding, nanoparticle reporters that provide spectroscopic information, and other novel intracellular sensor devices to provide spectroscopic data on intracellular processes.

